

METTTLER (L.H.)

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FOLLOWING TYPHOID FEVER.

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REPRINTED FROM THE

New York Medical Journal  
*for March 9, 1895.*





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## SPONTANEOUS GANGRENE FOLLOWING TYPHOID FEVER.\*

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LITERATURE contains many isolated reports of cases of dry and moist gangrene following typhoid fever, but the systematic study of this occasional and sometimes fatal sequel is still wanting. The subject was first broached by Bourgeois d'Etampes, in 1857, before La Société médicale des hôpitaux de Paris. Dr. Charcellay, of the Hospital of Tours, had a case in 1843 in which the whole left side of the face underwent mortification. Patry many years ago referred to gangrene as a sequel of typhoid fever and associated it with an arteritis—a view in which Hayem could not concur. For so important a complication, it is surprising that so little mention has been made of it in the standard authorities. Reynolds, Bartholow, and Wilson do not allude to it at all. Flint states that he never saw a case, while Keen is sponsor for the assertion that Trousseau never saw a case. I find, however, that Trousseau referred to a case reported by Dr. Boudeau wherein gangrene of

\* Read before the Chicago Medical Society, January 21, 1895.

the right foot took place in a child ten years of age. Unlike either Patry or Hayem, he attributed the accompanying arteritis to the clot acting as a foreign body upon the walls of the blood-vessels. Murchison and Hutchinson each devote but a brief paragraph to its consideration. Broadbent and Liebermeister say nothing about it. Fagge merely mentions the possibility of a thrombus of the femoral vein with an attendant liability to pulmonary embolism. Strümpell makes no reference whatever to gangrene following enteric fever. Osler assigns a short and incomplete paragraph to it. Most of the works on surgery that I have consulted simply mention the possibility of its occurrence. The fullest treatment of the subject that I have been able to discover is W. W. Keen's Toner Lecture, which, however, is dated 1876.

And yet this is not such an uncommon sequel of typhoid fever as all this reticence on the part of the authorities would lead one to imagine. I have seen two well-marked cases—one in a child ten years of age, in which amputation of the right leg had to be performed; the other in a woman, seventy years of age, in which both femoral vein and artery were obstructed, ultimately causing death. Both cases have already been placed upon record.\* Out of one hundred and thirteen cases of gangrene following fever, collected by Dr. Keen, forty-three followed typhoid fever. Barchoud † has tabulated some twenty cases of arterial obstruction following typhoid fever, and of these eight proved fatal. During an epidemic of typhus and typhoid in Finland in 1865, Estlander saw thirty-four cases, all of which, however, followed typhus fever except one. Most of the writers who have considered the subject at all do not report more than one or two cases that have come under their

\* *Philadelphia Medical Times*, Feb. 19, 1887.

† *Paris Thesis*, 1881.



observation. As the result of a rapid glance through the more recent literature, I have made notes of cases reported by Sallès, Hanquet, Wedewsky, Gosse, Drewitt, Fränkel, Donkin, Newbolt, Cushing, Lucas-Championnière, Keim, Long, Koehn, Chew, Laporte, and Grancher.

Among the predisposing causes of this complication of typhoid fever are lowered body vitality, mental depression, and an unsanitary mode of life. It is more frequent, therefore, in epidemics and in times of disaster. Most of the cases occur prior to the middle period of life. In Keen's collected cases the ages varied from fifteen to twenty-five years. In my own two cases they were ten and seventy years of age. In those I have collected from the later literature they were from eleven to thirty-two years. As typhoid fever itself is a disease of the early half of life its complications would necessarily correspond. Both cases observed by me were in females. Of eighty-one cases of Keen's list, fifty-six were in males, twenty-five in females. Of nine patients in my list whose sex was reported, six were men, three were women. It is therefore predominant in the male sex. In both cases reported by me it occurred in the lower half of the body; in the calf of the right leg of the girl, in the right leg and part of the thigh of the woman. Out of ten of my collected cases the obstruction was discovered in the lower extremities, usually the left, in six instances, once in the left cheek, once in the mesenteric vessels, once in the left carotid. When it occurs in the cerebral arteries, the complication is usually classified among the neurotic, because of the hemiplegia that results. In one hundred and twenty-six of Keen's cases it took place seventy-seven times in the extremities, chiefly the lower, and in twenty-two cases in the peripheral districts of the vasomotor system, such as the ears, nose, and genitals. This clearly demonstrates that it is a complication of the peripheral vascular apparatus.

This peripheral distribution of the trouble led the earlier investigators to attribute it entirely to the weakened heart action and slackened blood current. Even to-day many lay great stress upon this mechanical cause. Keen is so convinced of the tremendous importance of this that he declares it "will more readily and rationally explain the causation of the gangrene," even in those rare cases where there is no clot, "than any specific action of the indefinite though undoubted poison of the fever." A moment's thought, however, ought to convince one of the inadequacy of such a simple explanation. Arterial obstruction with resulting gangrene is far too rare a complication to be attributed solely to a condition which obtains with almost invariable constancy in enteric fever. Except in the very mildest cases the typhoid heart always manifests a dangerous weakness until far into convalescence, and yet vascular obstruction occurs quite infrequently in the disease. We must not be misled by the fact that this complication usually appears in the third week of the fever, and not infrequently when convalescence has become well established, for there is still something more than mere blood stasis needed to account for its wide distribution, comparative infrequency, and insidious onset. In Wedewsky's case a symmetrical gangrene appeared two years after the attack of fever and was attributed "to the toxic action of the products of the activity of the typhoid bacillus."

Pathologists at the present time are generally agreed that the obstruction of an artery by a clot is in the vast majority of cases at least the cause of the gangrene, but as to the cause of the clot there is still a diversity of opinion. An endocarditis distributing emboli which finally become fastened in some narrowed portion of the arterial system, and so become the nuclei of the future thrombi, has been designated as one cause. If this were the case we should

expect the gangrene to appear in other parts of the body quite as frequently as in the lower extremities; but, as a matter of fact, out of a hundred and twenty-six localities affected in the cases cited by Dr. Keen, seventy-seven were in the extremities, and seventy-two of these in the legs. Furthermore, endocarditis, according to Wilson, is a very rare complication of typhoid fever. In neither of the two cases reported by me could the slightest indications of it be detected.

Another explanation of the appearance of the clot has been the combined effect of (a) "the altered blood"; (b) "the weakened heart"; and (c) "the mechanical difficulties in carrying on the circulation, especially in distant parts." While these may undoubtedly be powerful factors in assisting in its formation, it does not seem to me, when we study the history of the cases thus far reported, that any one of these conditions, or even all three combined, are immediately the cause of the clot. The same conditions are present in other severe forms of fever, such as pyæmia, puerperal fever, diphtheria, and pneumonia, and yet mortification of extensive areas due to an arterial obstruction is never so imminent as in typhoid fever. Moreover, in typhoid itself these conditions are very constant and well marked, but the gangrene, as Dr. Keen truly says, "is happily a rare complication." Let us consider for a moment each of these conditions, whose combined effect is said to produce the clot. Barié, writing in 1884 for the *Revue de médecine*, states that the spontaneous occlusion of an artery by what Virchow calls "marasmic clots," or clots due simply to a certain condition of the blood, "is almost impossible" in typhoid fever, because of the peculiar kind of change in the blood of that fever, represented by a "diminution of the hæmoglobin, of the red corpuscles, and plasma." And again, as Green says, "to whatever cause



it may be due, an increased tendency of the blood to coagulate is probably *never more than a predisposing cause of thrombosis.*" Thus the "altered condition of the blood," aside from the fact of its bearing a specific poison of a high degree of virulence, can not be accepted as any more than a predisposing cause of thrombosis, especially if the endothelium remains intact. Secondly, as to the "weakened heart," it needs but a moment's reflection to understand that this also is nothing but a predisposing cause in producing a retardation of the blood current. A weakened heart is characteristic of many other diseases in which gangrene is scarcely ever known to occur. Thirdly, as to the "mechanical difficulties in carrying on the circulation." This and the weakened heart condition act much in the same way to produce a stagnation of the current, a distended state of the arteries, and an impaired nutrition of the arterial walls, through a consequent abnormal condition of the vasa vasorum, the whole terminating in an arteritis of greater or less degree. But how are we to explain the tendency to gangrene that so generally accompanies typhoid fever—a fact upon which M. Behier laid marked stress so long ago as 1857—and its singular absence in other diseases in which arteritis of the same sort ought frequently to obtain, seeing that in them this condition of the heart and circulation is almost as common as in typhoid fever?

The more I have studied this question, the more am I convinced that the production of arterial thrombosis and subsequent gangrene in typhoid fever is due in by far the greater majority of cases to an endarteritis assisted by various mechanical factors. The immediate cause of this endarteritis is in all probability the fever poison in the blood in a condition of extreme virulence. It is the result of an intense toxæmia. That this is the state of the blood, or that this is its effect upon the inner lining of the arter-



ies, is established by the "almost constant muscular degeneration" which is so peculiar to typhoid, and which has been attributed to an *inflammatory obstruction* of the arteries supplying the muscular tissues. In this way do Hayem and Martin explain the myocarditis and subsequent softening of the heart muscle. Giraudeau attributes the degeneration of the general muscular system to an incipient myositis and that of the various viscera to the hæmorrhagic infarctions all produced by the same cause—viz., a primitive obliterating arteritis induced by a highly poisonous condition of the blood. Arteritis has been attributed to the poisoned blood state in variola (Brouardel), diphtheria and marsh miasm (Lancereaux, Verneuil), tuberculosis (Lancereaux), syphilis, and rheumatism. Inflammation of the arteries from this cause is not, therefore, an uncommon affair. Of a hundred and thirteen cases collected by Keen, however, it is seldom stated that the arterial walls were diseased. This may easily be accounted for by the comparatively incomplete autopsies that were often made in these cases. So many of these cases occur in private practice, and they are, moreover, so rare, that unfortunately post mortem examinations are hard to obtain. In neither of my cases was an autopsy permitted, though the symptoms in the case of the girl pointed obscurely to an endarteritis of the obstructed vessel. In Sallès's case it is expressly stated that there was an "obliterative arteritis," and in the more numerous cases of venous obstruction a phlebitis appears to have been a manifest cause. The signs of the arteritis, when it occurs, make their appearance first about the latter part of the third week, or the beginning of convalescence. The pain along the course of the vessel may be of a sharp, stinging character, or dull and aching. One patient likened it to the "stretching or tearing of the nerves of the limb." Movement, external pres-

sure, or simply the erect posture increases it. There is occasionally violent throbbing of the blood-vessel, not infrequently felt in parts of the body situated at a considerable distance from the inflamed artery. Finally, the pulse beat becomes hard and wiry. As the vessel becomes less and less permeable, and the blood supply of the contiguous tissues diminished, there will be noticed a slight lowering of the local temperature, oftentimes as much as several tenths of a degree. The skin assumes a bluish or violaceous hue, while its sensitiveness is considerably enhanced. All symptoms of arteritis, and especially endarteritis, are exceedingly obscure, pain being the most reliable, and this having to be carefully distinguished from the pain of neuralgia, phlebitis, and lymphangitis. It is from these obscure symptoms rather than from more exact autopsies that an obliterative arteritis has been given the credit of the formation of the clot. Among those who support the view of a general primitive arteritis occurring in typhoid fever, based upon the few autopsies made by themselves, may be mentioned Gigon, Hayem, Patry, Larroque, Behier, Bourdeau, Mercier, Maserell, and others. In view of this, as well as of the fact that "abnormality or removal of the endothelium is the essential condition" (Green) to the formation of the clot, it is difficult to harmonize the presence of the clot with the *reported* healthy condition of the arteries in so large a proportion of Dr. Keen's cases. I think we may safely conclude that the cause of gangrene following typhoid fever is an obliterative arteritis lighted up by a virulent toxæmia, and that its appearance and frequency are determined by the vitality of the patient's tissues, the degree of virulence of the blood-poison, and certain minor mechanical factors.

The prognosis depends upon so many attendant circumstances that it is difficult to form any decided conclusions. It is less favorable than gangrene under other conditions

by reason of the exhausted state of the patient produced by the attack of fever. Exhaustion practically destroyed both of my patients, though the little girl lived six weeks after the amputation. Of Barchoud's twenty cases, eight proved fatal. Barker and Cheyne have recorded a case in which death occurred two hours and a half after gangrene had begun in the nose. In a few cases of obstruction a collateral circulation has been established, and in a still smaller number there has been a restoration of the lumen of the obstructed vessel. It is more common, however, for a line of demarcation to appear after the lapse of a few weeks and Nature to relieve the patient of the mortified tissues. I need say nothing in regard to the prophylaxis and treatment of this complication of typhoid fever, as they differ in no respect from the treatment of gangrene under other circumstances.

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# The New York Medical Journal.

*A WEEKLY REVIEW OF MEDICINE.*

EDITED BY

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Subscription price, \$5.00 per annum. Volumes begin in January and July.

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PUBLISHED BY

D. APPLETON & CO., 72 Fifth Avenue, New York.

